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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,419	BARONE ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. The Provisional Application filed 3 March 2000 upon which priority is claimed provides adequate support under 35 U.S.C. 112 for claims 1-20 of this application.

Specification

2. The disclosure is objected to because of the following informalities: The specification is objected to because on page 18, lines 3 and 23-24, U.S. Patent Application No. 08/630,148 is defined as a co-pending application. The '148 application issued on 8 February 2000 which was prior to filing of Provisional Application 60/190,166 filed on 17 March 2000. Therefore, the '148 application was not co-pending with the instant application.

Appropriate correction is required.

Claim Objections

3. Claim 2 is objected to because in step (c), line 3, linked is misspelled "link".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-20 are indefinite in Claim 1 because the claim is drawn to a method of preparing a nucleic acid array but the claim does not recite method steps of array preparation. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6. It is suggested that Claim 1 be amended to recite positive and active method steps of array preparation.

b. Claims 1-20 are indefinite in Claim 1 for the recitation "said synthesizing" because the recitation lacks proper antecedent basis in the claim. It is suggested that Claim 1 be amended to provide proper antecedent basis e.g. replace "synthesizing" with "method".

c. Claim 2 is indefinite in line 1 for the recitation "said synthesizing" because the recitation lacks proper antecedent basis in Claim 1. It is suggested that Claim 2 be amended to provide proper antecedent basis e.g. replace "synthesizing" with "method".

d. Claim 2 is indefinite in step (b) for the recitation "attaching a nucleotide to a first region" because it is unclear whether the "first region" refers to the "a region" of step (a). It is suggested that Claim 2 be amended to clarify e.g. replace "first" with "said".

e. Claim 2 is indefinite in step (c), line 4, for the recitation "different from that used in step (b)" because "used" lacks proper antecedent basis in step (b) which attaches (not uses) the

nucleotide. It is suggested that Claim 2 be amended to provide proper antecedent basis e.g. replace "used" with "attached".

f. Claim 3 is indefinite in line 1 for the recitation "said synthesizing" because the recitation lacks proper antecedent basis in Claim 1. It is suggested that Claim 3 be amended to provide proper antecedent basis e.g. replace "synthesizing" with "method".

g. Claim 3 is indefinite because it is unclear whether the "first area" and "second area" of steps (a) and (b) are the same or different from "first area" and "second area" of steps (c) and (d). It is suggested that Claim 3 be amended to clarify.

h. Claims 12 and 13 are each indefinite for the recitation "wherein each different nucleic acid" because the recitation lacks proper antecedent basis in Claim 5. It is suggested that Claims 12 and 13 be amended to provide proper antecedent basis e.g. replace "each" with "a".

Claim Rejections - 35 USC § 102/103

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-20 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McGall et al (U.S. Patent No. 6,022,963, issued 8 February 2000).

Regarding Claim 1, McGall et al disclose a method of preparing a nucleic acid array on a support wherein each nucleic acid occupies a separate known region of the support said method comprising: contacting said support with protected nucleoside phosphoramidite monomers (Column 9, lines 5-38) wherein the protected nucleoside phosphoramidite monomers are "pure phosphoramidite" (Column 13, line 67-Column 14, line 24).

The preceding rejection is based on judicial precedent following In re Fitzgerald, 205 USPQ 594 because McGall et al is silent with regard the claimed "monomers having less than about 1 mole % phosphoramidite contaminant". However, the monomers recited in Claims 1-20 are deemed to be inherent in the "pure phosphoramidites" in McGall et al because a "pure" substance inherently lacks impurities i.e. contaminants . Therefore, the "pure phosphoramidites" disclosed by McGall et al inherently has less than about 1 mole % of phosphoramidite contaminant as claimed.

Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the monomers of McGall et al using routine experimentation to derive monomers having less than 1 mole % phosphoramidite contaminants as claimed to thereby optimize reagents to thereby maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

"[T]he mere purity of a product, by itself, does not render the product unobvious." *Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989). The Board held that the burden of

persuasion was on appellant to show that the claimed product exhibited unexpected properties compared with that of the prior art. The Board further noted that "no objective evidence has been provided establishing that no method was known to those skilled in this field whereby the claimed material might have been synthesized." (10 USPQ2d at 1926.). Factors to be considered in determining whether a purified form of an old product is obvious over the prior art include whether the claimed chemical compound or composition has the same utility as closely related materials in the prior art, and whether the prior art suggests the particular form or structure of the claimed material or suitable methods of obtaining that form or structure. see MPEP, 2144.05. The method of McGall et al has the same utility as the claimed method i.e. nucleic acid array preparation and McGall et al specifically teaches "pure phosphoramidites", methods of making them and methods of using them.

The burden is on applicant to show that the claimed monomers having less than about 1 mole % phosphoramidite contaminant are either different or non-obvious over that of McGall et al.

Regarding Claim 2, McGall et al disclose the method further comprising: activating a region of the support; attaching a nucleotide to a first region said nucleotide having a masked reactive site linked to a protecting group; repeating the activating and attaching on other regions of the support whereby each of said other regions has bound thereto another nucleotide comprising a masked reactive site linked to a protective group; removing the protective group from one of the nucleotides bound to one of the regions of the support to provide a region bearing a nucleotide having an unmasked reactive site; binding an additional nucleotide to the nucleotide to the nucleotide with an unmasked reactive site; and repeating the removing and binding until a desired plurality of nucleic acid is synthesized, each occupying separate known regions of the support (Column 9, lines 5-38 and Claim 25) wherein the phosphoramidite is pure (Column 14, lines 1-23).

Regarding Claim 3, McGall et al disclose the method further comprising: generating a pattern of light and dark areas by selectively irradiating at least a first area of a surface said surface comprising immobilized nucleotides said nucleotides capped with a photoremovable groups without irradiating at least a second area of said surface to remove said protective group simultaneously contacting said first area and said second area with a first nucleotide to couple said first nucleotide to said immobilized nucleotides and not it said second area said first nucleotide capped with said photoremovable protective group; generating another pattern of light and dark areas by selectively irradiating with light at least a part of said first area and at least a part of a second area to remove said protective group; simultaneously contacting said first area and said second areas with a second nucleotide to couple said second nucleotide to said immobilized nucleotides; performing additional irradiating and nucleotide contacting and coupling steps so that a matrix array of at least 100 nucleic acids having different sequences is formed on said support (Column 9, lines 5-38 and Claim 25).

Regarding Claim 4, McGall et al disclose the method of Claim 1 wherein the protected nucleoside phosphoramidite monomers are "pure phosphoramidite" (Column 13, line 67-Column 14, line 24).

The preceding rejection is based on judicial precedent following In re Fitzgerald, 205 USPQ 594 because McGall et al is silent with regard the claimed "monomers having less than about 1 mole % phosphoramidite contaminant". However, the monomers recited in Claim 4 are deemed to be inherent in the "pure phosphoramidites" in McGall et al because a "pure" substance inherently lacks impurities i.e. contaminants . Therefore, the "pure phosphoramidites" disclosed by McGall et al inherently has less than about 1 mole % of phosphoramidite contaminant as claimed.

Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the monomers of McGall et al using routine experimentation to derive monomers having less than 0.2 mole % phosphoramidite

contaminants as claimed to thereby optimize reagents to thereby maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

The burden is on applicant to show that the claimed monomers having less than about 0.2 mole % phosphoramidite contaminant are either different or non-obvious over that of McGall et al.

Regarding Claim 5, McGall et al disclose the method having the claimed formula wherein B is a member selected from the group consisting of adenine, guanine, thymine, cytosine, uracil and analogs thereof; R is a member selected from the group consisting of hydrogen, hydroxyl, protected hydroxy, halogen, and alkoxy; P is a phosphoramidite group; and PG is a photoremovable group (Column 5, line 46-Column 6, line 50 and Fig. 1).

Regarding Claim 6, McGall et al disclose the method wherein B is selected from the group consisting of adenine, guanine, thymine, cytosine and R is a hydrogen (Column 5, line 46-Column 6, line 50 and Fig. 1).

Regarding Claim 7, McGall et al disclose the method of Claim 5 wherein said array comprises at least 10 different nucleic acids (Column 10, lines 33-38).

Regarding Claim 8, McGall et al disclose the method of Claim 5 wherein said array comprises at least 100 different nucleic acids (Column 10, lines 33-38).

Regarding Claim 9, McGall et al disclose the method of Claim 5 wherein said array comprises at least 1,000 different nucleic acids (Column 10, lines 33-38).

Regarding Claim 10, McGall et al disclose the method of Claim 5 wherein said array comprises at least 10,000 different nucleic acids (Column 10, lines 33-38).

Regarding Claim 11, McGall et al disclose the method of Claim 5 wherein said array comprises at least 100,000 different nucleic acids (Column 10, lines 33-38).

Regarding Claim 12, McGall et al disclose the method of Claim 5 wherein each different nucleic acid is in a region having an area of less than about 1 cm^2 (Column 10, lines 39-40).

Regarding Claim 13, McGall et al disclose the method of Claim 5 wherein each different nucleic acid is in a region having an area of less than about 1 mm^2 (Column 10, lines 39-40).

Regarding Claim 14, McGall et al disclose the method of Claim 5 wherein the protected nucleoside phosphoramidite monomers are "pure phosphoramidite" (Column 13, line 67-Column 14, line 24).

Regarding Claim 15, McGall et al disclose the method of Claim 5 wherein B is selected from the group consisting of adenine, guanine, thymine, cytosine and R is a hydrogen (Column 5, line 46-Column 6, line 50 and Fig. 1) wherein the protected nucleoside phosphoramidite monomers are "pure phosphoramidite" (Column 13, line 67-Column 14, line 24).

Regarding Claim 16, McGall et al disclose the method of Claim 5 wherein B is selected from the group consisting of adenine, guanine, thymine, cytosine; R is a hydrogen; PG is MeNPOC (Column 5, line 46-Column 6, line 50; Column 15, Table 3 and Fig. 1) wherein the protected nucleoside phosphoramidite monomers are "pure phosphoramidite" (Column 13, line 67-Column 14, line 24).

Regarding Claim 17, McGall et al disclose the method of Claim 5 wherein B is selected from the group consisting of adenine, guanine, thymine, cytosine; R is a hydrogen; PG is MeNPOC; P is P-(OCH_2HC_2CN)N(iPr)2 (Column 5, line 46-Column 6, line 50 and Fig. 1) wherein the protected nucleoside phosphoramidite monomers are "pure phosphoramidite" (Column 13, line 67-Column 14, line 24).

The preceding rejection of Claims 14-17 is based on judicial precedent following In re Fitzgerald, 205 USPQ 594 because McGall et al is silent with regard the claimed "monomers having less than about 1 mole % phosphoramidite contaminant". However, the monomers

recited in Claims 1-20 are deemed to be inherent in the "pure phosphoramidites" in McGall et al because a "pure" substance inherently lacks impurities i.e. contaminants . Therefore, the "pure phosphoramidites" disclosed by McGall et al inherently has less than about 1 mole % of phosphoramidite contaminant as claimed.

Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the monomers of McGall et al using routine experimentation to derive monomers having less than 0.2 mole % phosphoramidite contaminants as claimed to thereby optimize reagents to thereby maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

The burden is on applicant to show that the claimed monomers having less than about 0.2 mole % phosphoramidite contaminant are either different or non-obvious over that of McGall et al.

Regarding Claims 18-20, McGall et al disclose nucleic acid arrays prepared by the methods of Claims 1, 5 and 17 (Column 10, lines 14-40).

Claim Rejections - 35 USC § 102/103

9. Claims 1-15 and 18-20 are rejected under 35 U.S.C. 103(a) as obvious over Fodor et al (U.S. Patent No. 5,800,992, issued 1 September 1998) in view of Srivastava et al (U.S. Patent No. 5,525,719, issued 11 June 1996).

Regarding Claim 1, Fodor et al teach a method of preparing a nucleic acid array on a support wherein each nucleic acid occupies a separate known region of the support said

method comprising: contacting said support with protected nucleoside phosphoramidite monomers (Column 38, line 52-Column 44, line 38) but they do not teach the purity of the phosphoramidite monomers. However, phosphoramidite monomers having less than 1 mole % contamination was well known in the art at the time the claimed invention was made as taught by Srivastava et al (Column 4, line 57-Column 5, line 41) who teach that pure phosphoramidite monomers are critical for synthesizing nucleic acids to be used in biological applications (Column 2, lines 1-21).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the pure monomers of Srivastava et al to the monomers of Fodor et al to thereby accurately synthesize nucleic acids on the support based on their critical importance in biological applications as taught by Srivastava et al (Column 2, lines 1-21).

Additionally, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the monomers of Fodor et al using routine experimentation to derive monomers having less than 1 mole % phosphoramidite contaminants as claimed to thereby optimize reagents to thereby maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

"[T]he mere purity of a product, by itself, does not render the product unobvious." *Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989). The Board held that the burden of persuasion was on appellant to show that the claimed product exhibited unexpected properties compared with that of the prior art. The Board further noted that "no objective evidence has been provided establishing that no method was known to those skilled in this field whereby the claimed material might have been synthesized." (10 USPQ2d at 1926.). Factors to be considered in determining whether a purified form of an old product is obvious over the prior art include whether the claimed chemical compound or composition has the same utility as

closely related materials in the prior art, and whether the prior art suggests the particular form or structure of the claimed material or suitable methods of obtaining that form or structure. see MPEP, 2144.05. The method of Fodor et al has the same utility as the claimed method i.e. nucleic acid array preparation. Therefore, the claimed monomers are obvious over the monomers Fodor et al in view of the teaching of Srivastava et al.

Regarding Claim 2, Fodor et al teach the method further comprising: activating a region of the support; attaching a nucleotide to a first region said nucleotide having a masked reactive site linked to a protecting group; repeating the activating and attaching on other regions of the support whereby each of said other regions has bound thereto another nucleotide comprising a masked reactive site linked to a protective group; removing the protective group from one of the nucleotides bound to one of the regions of the support to provide a region bearing a nucleotide having an unmasked reactive site; binding an additional nucleotide to the nucleotide to the nucleotide with an unmasked reactive site; and repeating the removing and binding until a desired plurality of nucleic acid is synthesized, each occupying separate known regions of the support (Column 38, line 52-Column 44, line 38).

Regarding Claim 3, Fodor et al teach the method further comprising: generating a pattern of light and dark areas by selectively irradiating at least a first area of a surface said surface comprising immobilized nucleotides said nucleotides capped with a photoremovable groups without irradiating at least a second area of said surface to remove said protective group simultaneously contacting said first area and said second area with a first nucleotide to couple said first nucleotide to said immobilized nucleotides and not it said second area said first nucleotide capped with said photoremovable protective group; generating another pattern of light and dark areas by selectively irradiating with light at least a part of said first area and at least a part of a second area to remove said protective group; simultaneously contacting said first area and said second areas with a second nucleotide to couple said second nucleotide to said immobilized nucleotides; performing additional irradiating and nucleotide contacting and

coupling steps so that a matrix array of at least 100 nucleic acids having different sequences is formed on said support (Column 38, line 52-Column 44, line 38).

Regarding Claim 4, Fodor et al teach the method of Claim 1 comprising protected nucleoside phosphoramidite monomers are "pure phosphoramidite" (Column 44, lines 30-38) but they do not teach the purity of the phosphoramidite monomers. However, phosphoramidite monomers having less than 1 mole % contamination was well known in the art at the time the claimed invention was made as taught by Srivastava et al (Column 4, line 57-Column 5, line 41) who teach that pure phosphoramidite monomers are critical for synthesizing nucleic acids to be used in biological applications (Column 2, lines 1-21).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the pure monomers of Srivastava et al to the monomers of Fodor et al to thereby accurately synthesize nucleic acids on the support based on their critical importance in biological applications as taught by Srivastava et al (Column 2, lines 1-21).

Regarding Claim 5, Fodor et al teach the method having the claimed formula wherein B is a member selected from the group consisting of adenine, guanine, thymine, cytosine, uracil and analogs thereof; R is a member selected from the group consisting of hydrogen, hydroxyl, protected hydroxy, halogen, and alkoxy; P is a phosphoramidite group; and PG is a photoremovable group (Column 44, lines 1-38).

Regarding Claim 6, Fodor et al teach disclose the method wherein B is selected from the group consisting of adenine, guanine, thymine, cytosine and R is a hydrogen (Column 4, lines 1-32).

Regarding Claim 7, Fodor et al teach the method of Claim 5 wherein said array comprises at least 10 different nucleic acids (Column 7, lines 51-67).

Regarding Claim 8, Fodor et al teach the method of Claim 5 wherein said array comprises at least 100 different nucleic acids (Column 7 lines 51-67).

Regarding Claim 9, Fodor et al teach the method of Claim 5 wherein said array comprises at least 1,000 different nucleic acids (Column 7, lines 51-67).

Regarding Claim 10, Fodor et al teach the method of Claim 5 wherein said array comprises at least 10,000 different nucleic acids (Column 7, lines 51-67).

Regarding Claim 11, Fodor et al teach the method of Claim 5 wherein said array comprises at least 100,000 different nucleic acids (Column 7, lines 51-67).

Regarding Claim 12, Fodor et al teach the method of Claim 5 wherein each different nucleic acid is in a region having an area of less than about 1 cm^2 (Column 7, lines 51-67).

Regarding Claim 13, Fodor et al teach the method of Claim 5 wherein each different nucleic acid is in a region having an area of less than about 1 mm^2 (Column 7, lines 51-67).

Regarding Claim 14, Fodor et al teach the method of Claim 5 comprising protected nucleoside phosphoramidite monomers (Column 44, lines 1-38) but they do not teach the purity of the phosphoramidite monomers. However, phosphoramidite monomers having less than 1 mole % contamination was well known in the art at the time the claimed invention was made as taught by Srivastava et al (Column 4, line 57-Column 5, line 41) who teach that pure phosphoramidite monomers are critical for synthesizing nucleic acids to be used in biological applications (Column 2, lines 1-21).

Regarding Claim 15, Fodor et al teach the method of Claim 5 wherein B is selected from the group consisting of adenine, guanine, thymine, cytosine and R is a hydrogen (Column 44, lines 1-38) comprising protected nucleoside phosphoramidite monomers but they do not teach the purity of the phosphoramidite monomers. However, phosphoramidite monomers having less than 1 mole % contamination was well known in the art at the time the claimed invention was made as taught by Srivastava et al (Column 4, line 57-Column 5, line 41) who teach that pure phosphoramidite monomers are critical for synthesizing nucleic acids to be used in biological applications (Column 2, lines 1-21).

Regarding the rejection of Claims 14 and 15, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the monomers of Fodor et al using routine experimentation to derive monomers having less than 0.2 mole % phosphoramidite contaminants as claimed to thereby optimize reagents to thereby maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claims 18-20, Fodor et al teach nucleic acid arrays prepared by the methods of Claims 1, 5 and 17 (Column 6,lines 23-48).

10. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as obvious over Fodor et al (U.S. Patent No. 5,800,992, issued 1 September 1998) in view of Srivastava et al (U.S. Patent No. 5,525,719, issued 11 June 1996) and Pirrung et al (U.S. Patent No. 5,908,926, issued 1 June 1999).

Regarding Claim 16, Fodor et al teach a method of preparing a nucleic acid array on a support wherein each nucleic acid occupies a separate known region of the support said method comprising: contacting said support with protected nucleoside phosphoramidite monomers (Column 38, line 52-Column 44, line 38) wherein B is selected from the group consisting of adenine, guanine, thymine, cytosine; R is a hydrogen; (Column 44, lines 1-38) comprising protected nucleoside phosphoramidite monomers but they do not teach the purity of the phosphoramidite monomers. However, phosphoramidite monomers having less than 1 mole % contamination was well known in the art at the time the claimed invention was made as taught by Srivastava et al (Column 4, line 57-Column 5, line 41) who teach that pure

phosphoramidite monomers are critical for synthesizing nucleic acids to be used in biological applications (Column 2, lines 1-21). Fodor et al do not teach PG is MeNPOC. However, MeNPOC photoremovable protective groups were well known in the art a the time the claimed invention was made as taught by Pirrung et al who teach a similar method of preparing a nucleic acid array wherein the photoremovable protective group is MeNPOC (Column 3, line 51-Column 4, line 5). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the MeNPOC protective group of Pirrung et al to the similar photoremovable protective groups of Fodor et al based on similarity of functionality and based on available reagents for the obvious benefits of economy of reagents. The courts have stated with regard to chemical homologs that the greater the physical and chemical similarities between the claimed species and any species disclosed in the prior art, the greater the expectation that the claimed subject matter will function in an equivalent manner (see *Dillon*, 99 F.2d at 696, 16 USPQ2d at 1904).

Regarding Claim 17, Fodor et al teach the method of Claim 5 wherein B is selected from the group consisting of adenine, guanine, thymine, cytosine; R is a hydrogen; P is P-(OCH_2HC_2CN)N(iPr)2 comprising protected nucleoside phosphoramidite monomers (Column 44, lines 1-38) but they do not teach the purity of the phosphoramidite monomers. However, phosphoramidite monomers having less than 1 mole % contamination was well known in the art at the time the claimed invention was made as taught by Srivastava et al (Column 4, line 57-Column 5, line 41) who teach that pure phosphoramidite monomers are critical for synthesizing nucleic acids to be used in biological applications (Column 2, lines 1-21). Fodor et al do not teach PG is MeNPOC. However, MeNPOC photoremovable protective groups were well known in the art a the time the claimed invention was made as taught by Pirrung et al who teach a similar method of preparing a nucleic acid array wherein the photoremovable protective group is MeNPOC (Column 3, line 51-Column 4, line 5). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the

MeNPOC protective group of Pirrung et al to the similar photoremovable protective groups of Fodor et al based on similarity of functionality and based on available reagents for the obvious benefits of economy of reagents. The courts have stated with regard to chemical homologs that the greater the physical and chemical similarities between the claimed species and any species disclosed in the prior art, the greater the expectation that the claimed subject matter will function in an equivalent manner (see *Dillon*, 99 F.2d at 696, 16 USPQ2d at 1904).

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-5, 9-14 and 24-29 of U.S. Patent No. 6,022,963. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods of synthesizing a plurality of nucleic acids on a support and differ only in the instant claims are drawn to synthesis using phosphoramidite monomers having less than about 1 mole % phosphoramidite contaminant. However, the monomers recited in Claims 1-17 are deemed to be inherent in the "pure phosphoramidites" in McGall et al because a "pure" substance inherently lacks impurities i.e. contaminants . Therefore, the "pure phosphoramidites" disclosed by McGall et al inherently has less than about 1 mole % of phosphoramidite contaminant as claimed.

Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the monomers of McGall et al using routine experimentation to derive monomers having less than 1 mole % phosphoramidite contaminants as claimed to thereby optimize reagents to thereby maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

The burden is on applicant to show that the claimed monomers having less than about 0.2 mole % phosphoramidite contaminant are either different or non-obvious over that of McGall et al.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
June 27, 2002